

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY
(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

REC'D 23 JAN 2007

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| Applicant's or agent's file reference 56815-5002WO | FOR FURTHER ACTION | | See Form PCT/IPEA/416 |
| International application No. PCT/US05/08957 | International filing date (day/month/year) 18 March 2005 (18.03.2005) | Priority date (day/month/year) 31 March 2004 (31.03.2004) | |
| International Patent Classification (IPC) or national classification and IPC IPC: A61K 38/24 (2006.01); G01 N 33/574 USPC: 435/7.23 | | | |
| Applicant TROPHOGEN, INC. | | | |
| <p>1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of <u>4</u> sheets, including this cover sheet.</p> <p>3. This report is also accompanied by ANNEXES, comprising:</p> <p>a. <input type="checkbox"/> (sent to the applicant and to the International Bureau) a total of ___ sheets, as follows:</p> <p><input type="checkbox"/> sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).</p> <p><input type="checkbox"/> sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.</p> <p>b. <input type="checkbox"/> (sent to the International Bureau only) a total of (indicate type and number of electronic carrier(s)) _____, containing a sequence listing and/or tables related thereto, in electronic form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).</p> <p>4. This report contains indications relating to the following items:</p> <p><input checked="" type="checkbox"/> Box No. I Basis of the report</p> <p><input type="checkbox"/> Box No. II Priority</p> <p><input type="checkbox"/> Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</p> <p><input type="checkbox"/> Box No. IV Lack of unity of invention</p> <p><input checked="" type="checkbox"/> Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</p> <p><input type="checkbox"/> Box No. VI Certain documents cited</p> <p><input checked="" type="checkbox"/> Box No. VII Certain defects in the international application</p> <p><input type="checkbox"/> Box No. VIII Certain observations on the international application</p> | | | |
| Date of submission of the demand 26 October 2005 (26.10.2005) | | Date of completion of this report 14 NOVEMBER 2006 | |
| Name and mailing address of the IPEA/ US Mail Stop PCT, Attn: IPEA/US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (571) 273-3201 | | Authorized officer Christina Borgeest <i>Christina Borgeest</i> Telephone No. 571-272-1600 | |

Form PCT/IPEA/409 (cover sheet) (April 2005)

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.

PCT/US05/08957

Box No. I Basis of the report

1. With regard to the language, this report is based on:

- ☒ the international application in the language in which it was filed.
- ☐ a translation of the international application into _____, which is the language of a translation furnished for the purposes of:
- ☐ international search (under Rules 12.3 and 23.1(b))
 - ☐ publication of the international application (under Rule 12.4(a))
 - ☐ international preliminary examination (under Rules 55.2(a) and/or 55.3(a))

2. With regard to the elements of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

- ☐ the international application as originally filed/furnished
- ☒ the description:
pages 1-25 as originally filed/furnished
pages* NONE received by this Authority on _____
pages* NONE received by this Authority on _____
- ☒ the claims:
pages 26-33 as originally filed/furnished
pages* NONE as amended (together with any statement) under Article 19
pages* NONE received by this Authority on _____
pages* NONE received by this Authority on _____
- ☒ the drawings:
pages 1 as originally filed/furnished
pages* NONE received by this Authority on _____
pages* NONE received by this Authority on _____
- ☐ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing.

3. ☒ The amendments have resulted in the cancellation of:

- ☒ the description, pages N/A
- ☒ the claims, Nos. N/A
- ☒ the drawings, sheets/figs N/A
- ☒ the sequence listing (*specify*): N/A
- ☒ any table(s) related to the sequence listing (*specify*): N/A

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

- ☐ the description, pages _____
- ☐ the claims, Nos. _____
- ☐ the drawings, sheets/figs _____
- ☐ the sequence listing (*specify*): _____
- ☐ any table(s) related to the sequence listing (*specify*): _____

* If item 4 applies, some or all of those sheets may be marked "superseded."

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Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

| | | |
|-------------------------------|-----------------------------------|-----|
| Novelty (N) | Claims <u>17-19, 21-22, 28-75</u> | YES |
| | Claims <u>1-16, 20, 23-27</u> | NO |
| Inventive Step (IS) | Claims <u>28-50</u> | YES |
| | Claims <u>1-27, 51-75</u> | NO |
| Industrial Applicability (IA) | Claims <u>1-75</u> | YES |
| | Claims <u>NONE</u> | NO |

2. Citations and Explanations (Rule 70.7)

1. Claims 1-16, 20, 23-27 lack novelty under PCT Article 33(2) as being anticipated by WO 00/17360 (University of Maryland, Baltimore, Weintraub et al., published 30 March 2000). Weintraub et al. teach modified glycoprotein hormones that can be used for imaging cells, treatment for various diseases or detection of analytes that interfere with the binding of the modified glycoprotein hormone and its receptor at p. 3, 2nd-3rd paragraphs, pps. 38-45, whole pages, pps. 49-53, whole pages (TSH and TSH-related disorders); pps. 54-61, whole pages (hCG and hCG-related disorders); pps. 61-67 (LH and LH-related disorders); pps. 67-74 under Diagnostic and Therapeutic Uses (FSH and FSH-related Disorders). Note that in US practice, the phrase, "a method of imaging cells", would be treated as a preamble and given little weight for the purpose of prior art if there is no recitation of a method step within the claim.

2. Claims 1, 15-19, 21-23 lack an inventive step under PCT Article 33(3) as being obvious over the prior art as applied in the immediately preceding paragraph and further in view of F. Stacul (Euro Radiol. 2001; 11: 690-697). Stacul discloses a variety of ionic and nonionic contrast agents for the purpose of imaging at p. 691, Tables 1-3). Imaging cells, for instance, via X-ray or MRI, is old in the art, as are the contrast agents. In addition, the claims recite "or combinations thereof", making the interpretation of the claims very broad, thus the claims cannot escape the prior art.

3. Claims 51-75 lack an inventive step under PCT Article 33(3) as being obvious over the prior art as applied in paragraph 1 above and further in view of WO 97/423322 (US Government, Szkudlinkski et al., published 13 November 1997). Szkudlinkski et al. disclose the claimed modified glycoprotein hormones as well as assays for determining glycoprotein hormone activity and binding. In addition, Weintraub et al. disclose that the recited hormones could be used for diagnosis.

4. Claims 28-50 meet the criteria set out in PCT Article 33(2)-(3), because the prior art does not teach or fairly suggest a fusion or chimeric protein consisting of a modified glycoprotein hormone having at least one mutation and the drugs recited in claims 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, or 49.

5. Claims 1-75 meet the criteria set out in PCT Article 33(4), and thus have industrial applicability because the subject matter claimed can be made or used in industry.

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Box No. VII Certain defects in the international application

The following defects in the form or contents of the international application have been noted:

Claim 18 is objected to under PCT Rule 66.2(a)(iii) as containing the following defect(s) in the form or contents thereof: "diaztrizoate" should be spelled "diatrizoate."